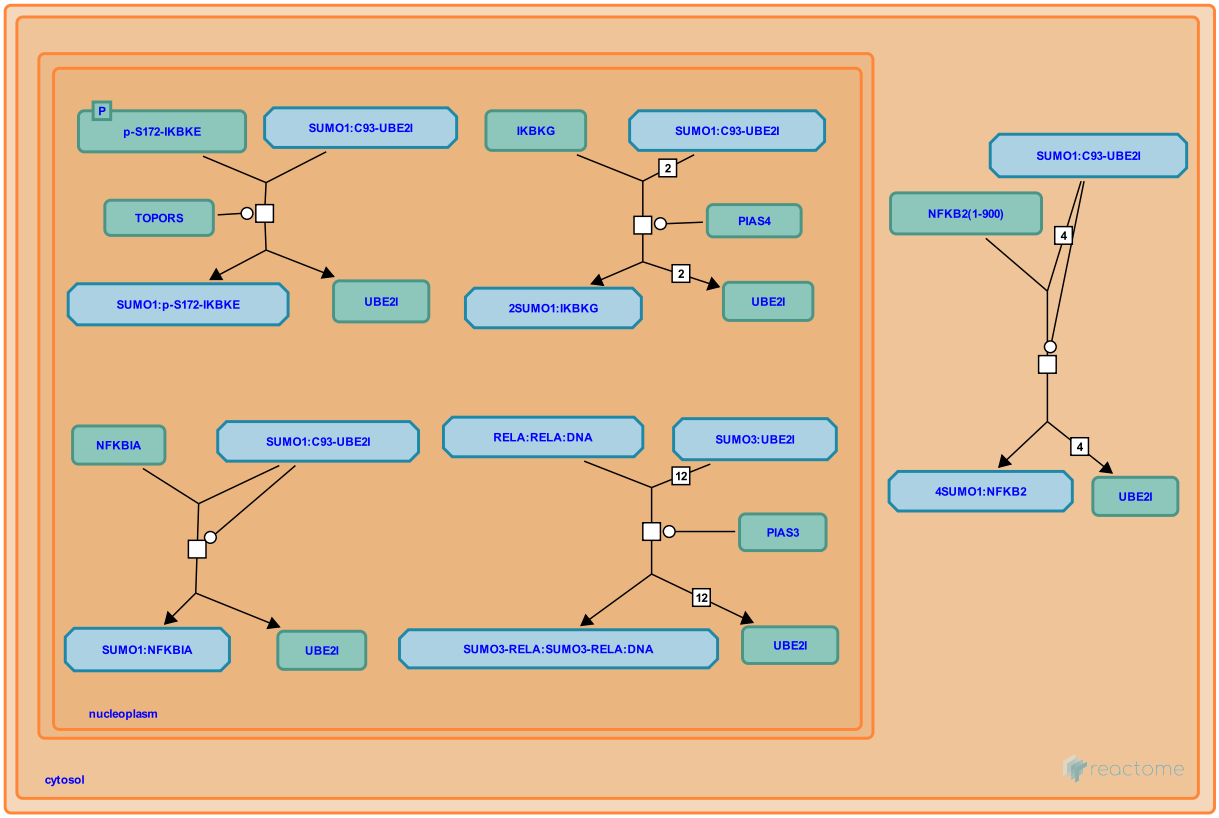
SUMOylation of immune response proteins



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19/08/2021

Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

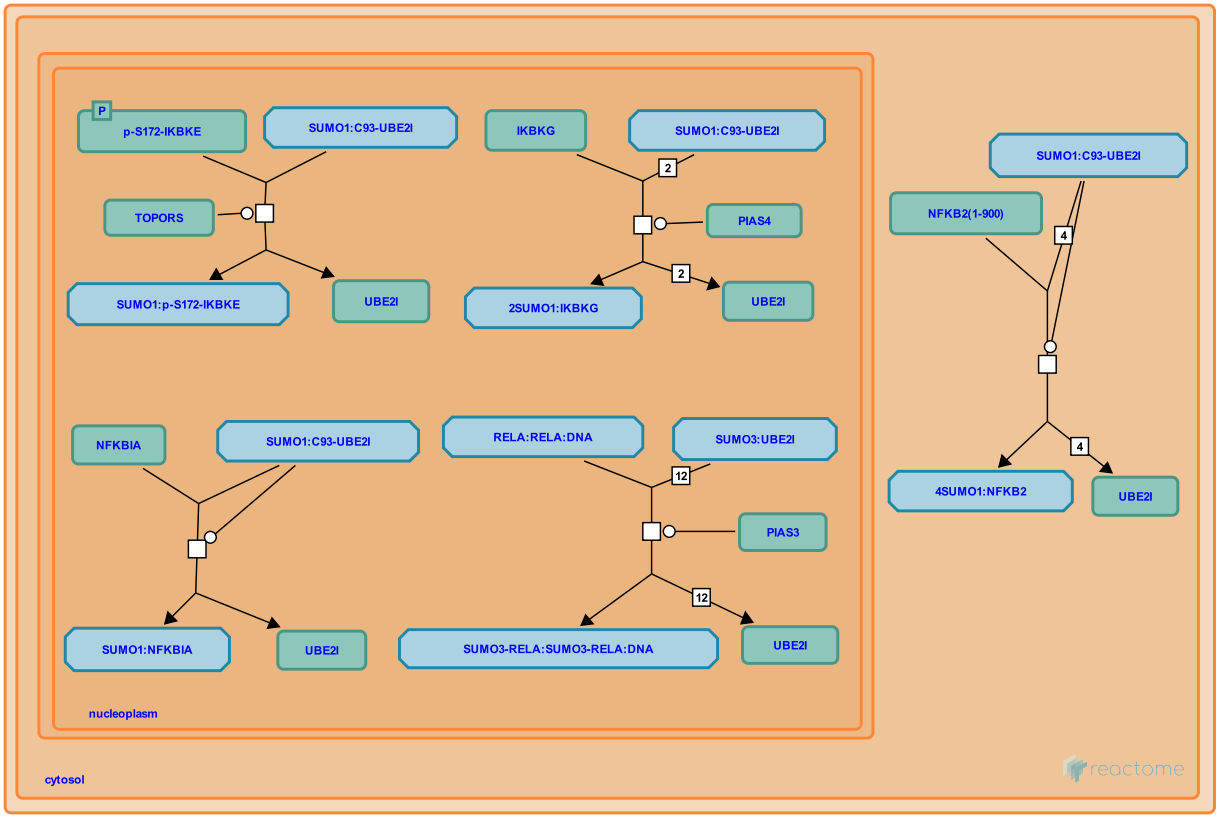
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

SUMOylation of immune response proteins ↗

Stable identifier: R-HSA-4755510

Compartments: nucleoplasm, cytosol



NF-kappaB transcription factors are sequestered in the cytosol due to their association with IkappaB. During activation of NF-kappaB, IKK phosphorylates IkappaB, releasing NF-kappaB for importation into the nucleus. NF-kappaB transcription factors, the NFKBIA component of IkappaB, and subunits of the IKK complex can be SUMOylated (reviewed in Kracklauer and Schmidt 2003, Liu et al. 2013). SUMOylations of IkappaB, NFKBIA, and RELA inhibit NF-kappaB signaling; SUMOylation of NFKB2 is required for proteolytic processing.

Literature references

Kracklauer, MP., Schmidt, C. (2003). At the crossroads of SUMO and NF-kappaB. *Mol. Cancer, 2*, 39. ↗

Liu, X., Wang, Q., Chen, W., Wang, C. (2013). Dynamic regulation of innate immunity by ubiquitin and ubiquitin-like proteins. *Cytokine Growth Factor Rev., 24*, 559-70. ↗

Editions

2013-10-20	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

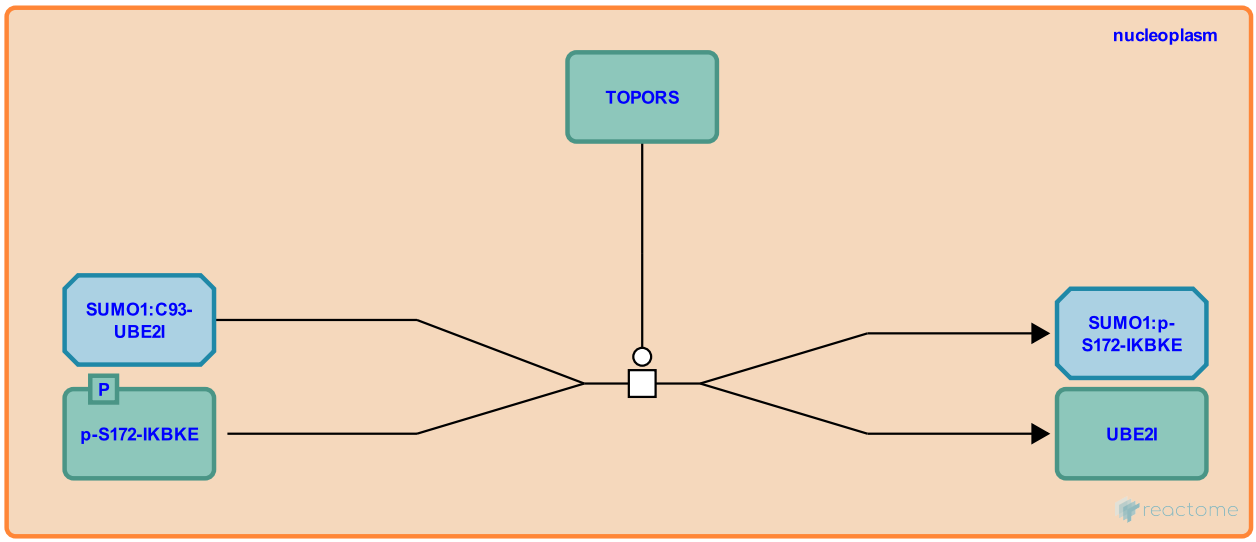
TOPORS SUMOylates IKBKE with SUMO1 ↗

Location: SUMOylation of immune response proteins

Stable identifier: R-HSA-4755478

Type: transition

Compartments: nucleoplasm



TOPORS SUMOylates phosphorylated IKBKE (IKKI, IKKE) with SUMO1 at lysine-231 (Renner et al. 2010). SUMOylation causes IKBKE to localize with PML in the nucleus and is required for IKBKE to trigger phosphorylation of NF-kappaB p65.

Literature references

Renner, F., Moreno, R., Schmitz, ML. (2010). SUMOylation-dependent localization of IKKepsilon in PML nuclear bodies is essential for protection against DNA-damage-triggered cell death. *Mol. Cell, 37*, 503-15. ↗

Editions

2013-10-20	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

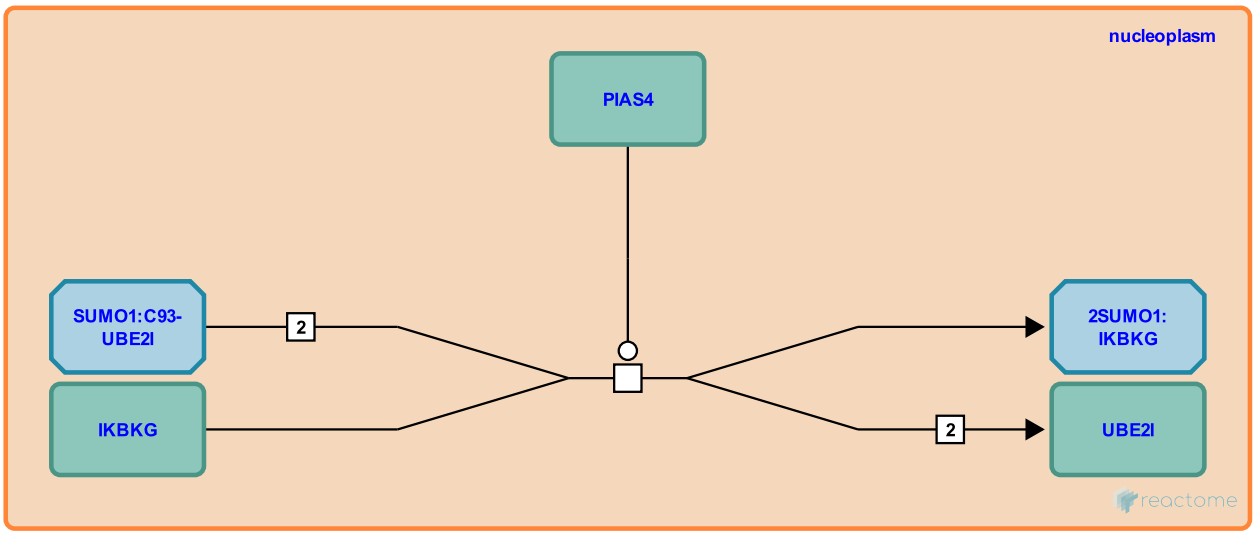
PIAS4 SUMOylates IKBKG with SUMO1 ↗

Location: SUMOylation of immune response proteins

Stable identifier: R-HSA-4755411

Type: transition

Compartments: nucleoplasm



PIAS4 SUMOylates IKBKG with SUMO1 at lysine-277 and lysine-309 (Huang et al. 2003, Mabb et al. 2006). SUMOylation occurs in the nucleus when IKBKG is unbound to IKK. The interaction between PIAS4 and IKBKG is increased by genotoxic stress. SUMOylation is independent of ATM.

Literature references

Mabb, AM., Wuerzberger-Davis, SM., Miyamoto, S. (2006). PIASy mediates NEMO sumoylation and NF-kappaB activation in response to genotoxic stress. *Nat. Cell Biol., 8*, 986-93. ↗

Huang, TT., Wuerzberger-Davis, SM., Wu, ZH., Miyamoto, S. (2003). Sequential modification of NEMO/IKKgamma by SUMO-1 and ubiquitin mediates NF-kappaB activation by genotoxic stress. *Cell, 115*, 565-76. ↗

Editions

2013-10-20	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

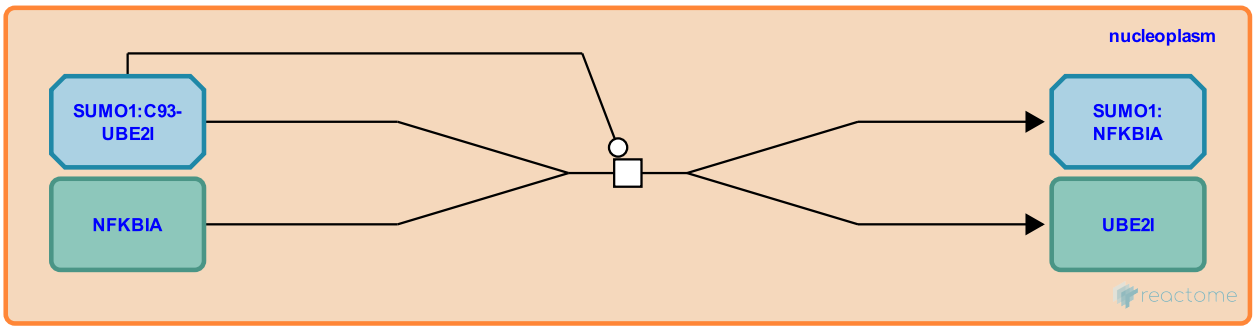
SUMOylation of NFKBIA with SUMO1 ↗

Location: SUMOylation of immune response proteins

Stable identifier: R-HSA-4656914

Type: transition

Compartments: nucleoplasm



NFKBIA (IKBA, IkappaBalpha) is SUMOylated at lysine-21 with SUMO1 (Desterro et al. 1998, Rodriguez et al. 2001, Liu et al. 2009). SUMOylation blocks ubiquitin-mediated proteolysis of NFKBIA and thereby inhibits NF-kappaB dependent transcription and acts as an anti-inflammatory. Adenosine signaling increases SUMOylation of NFKBIA with SUMO1. Nuclear import of NFKBIA is required for SUMOylation.

Literature references

Rodriguez, MS., Dargemont, C., Hay, RT. (2001). SUMO-1 conjugation in vivo requires both a consensus modification motif and nuclear targeting. *J. Biol. Chem., 276*, 12654-9. ↗

Desterro, JM., Rodriguez, MS., Hay, RT. (1998). SUMO-1 modification of IkappaBalpha inhibits NF-kappaB activation . *Mol. Cell, 2*, 233-9. ↗

Liu, Q., Li, J., Khoury, J., Colgan, SP., Ibla, JC. (2009). Adenosine signaling mediates SUMO-1 modification of IkappaBalpha during hypoxia and reoxygenation. *J. Biol. Chem., 284*, 13686-95. ↗

Editions

2013-10-03	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

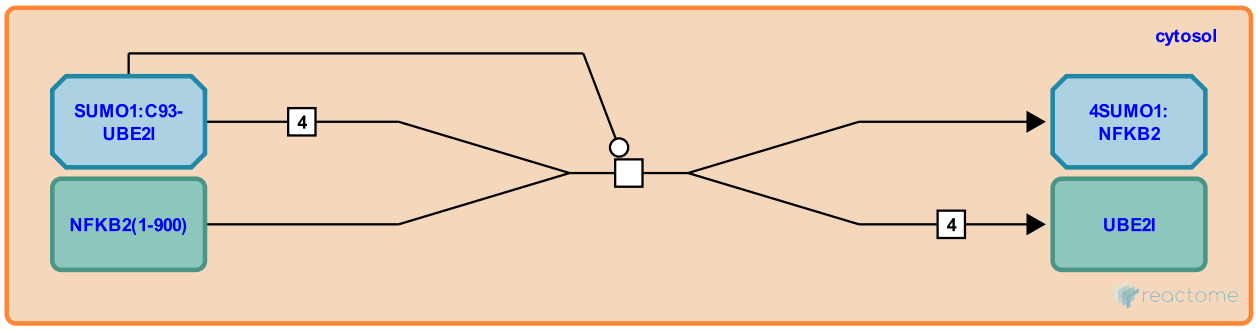
SUMOylation of NFKB2 with SUMO1 ↗

Location: SUMOylation of immune response proteins

Stable identifier: R-HSA-4755479

Type: transition

Compartments: cytosol



Unprocessed NFKB2 p100 is SUMOylated with SUMO1 at lysine-90, lysine-298, lysine-689, and lysine-863 (Vatsyayan et al. 2008). SUMOylation of p100 is required for phosphorylation of p100 prior to processing to yield p52. Blockage of SUMOylation consequently interferes with import of NFKB2 p52 into the nucleus.

Literature references

Vatsyayan, J., Qing, G., Xiao, G., Hu, J. (2008). SUMO1 modification of NF-kappaB2/p100 is essential for stimuli-induced p100 phosphorylation and processing. *EMBO Rep., 9*, 885-90. ↗

Editions

2013-10-20	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

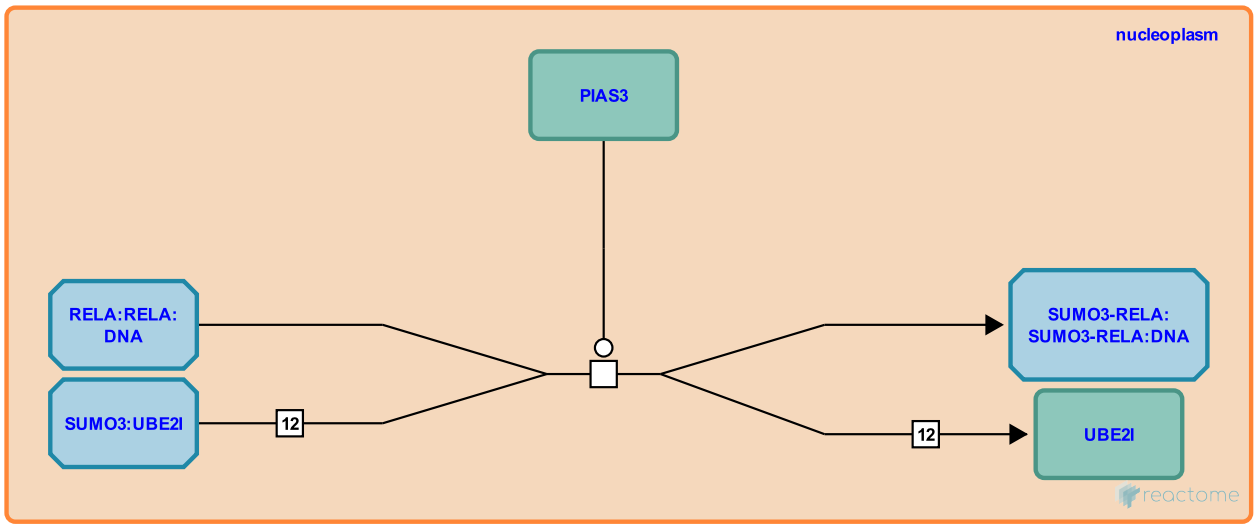
PIAS3 SUMOylates RELA with SUMO3 ↗

Location: SUMOylation of immune response proteins

Stable identifier: R-HSA-4755536

Type: transition

Compartments: nucleoplasm



PIAS3 SUMOylates RELA with SUMO3 at lysine-37, lysine-121, and lysine-122 (Liu et al. 2012, Hendriks et al. 2014). SUMOylation occurs when RELA is bound to NF-kB binding sites on DNA in the nucleus. SUMOylation represses transcriptional activity of RELA and is enhanced by NF-kB activation by TNFalpha.

Literature references

Liu, Y., Bridges, R., Wortham, A., Kulesz-Martin, M. (2012). NF-?B repression by PIAS3 mediated RelA SUMOylation. *PLoS ONE, 7*, e37636. ↗

Hendriks, IA., D'Souza, RC., Yang, B., Verlaan-de Vries, M., Mann, M., Vertegaal, AC. (2014). Uncovering global SUMOylation signaling networks in a site-specific manner. *Nat. Struct. Mol. Biol., 21*, 927-36. ↗

Editions

2013-10-20	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

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